# BETAMI-DANBLOCK

**RANDOMIZED DISCONTINUATION OF BETA-BLOCKERS AFTER MYOCARDIAL INFARCTION**

BETAMI Study
BEta-Blocker Treatment after Acute Myocardial Infarction

DANBLOCK

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# Disclosures

- **BETAMI-DANBLOCK: Investigator-initiated, supported only by public and independent non-profit foundations**

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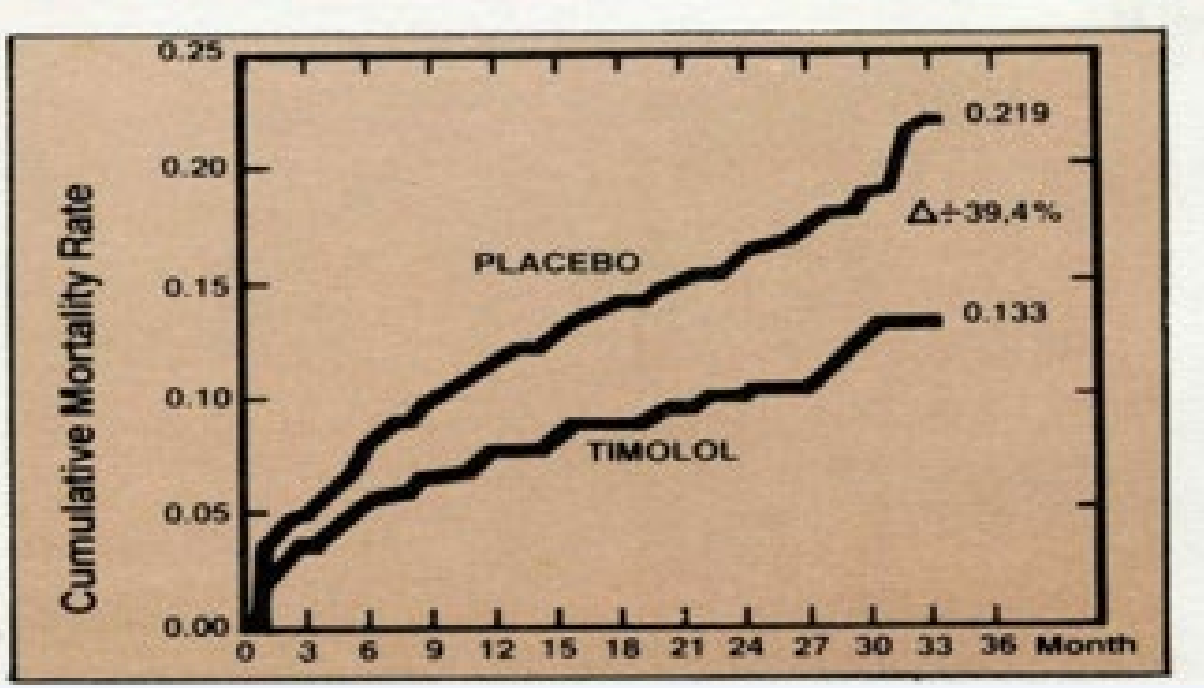
- DA: Grant support (to the Institution): BMS/Pfizer, Medtronic, Bayer, Roche-Diagnostics.

# Background

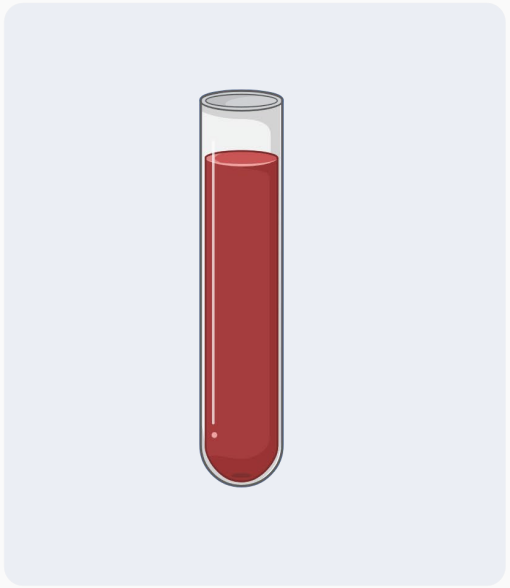
## A MULTICENTER STUDY ON TIMOLOL IN SECONDARY PREVENTION AFTER INFARCTION

By Terje R. Pedersen
The Norwegian
Multicenter Study Group

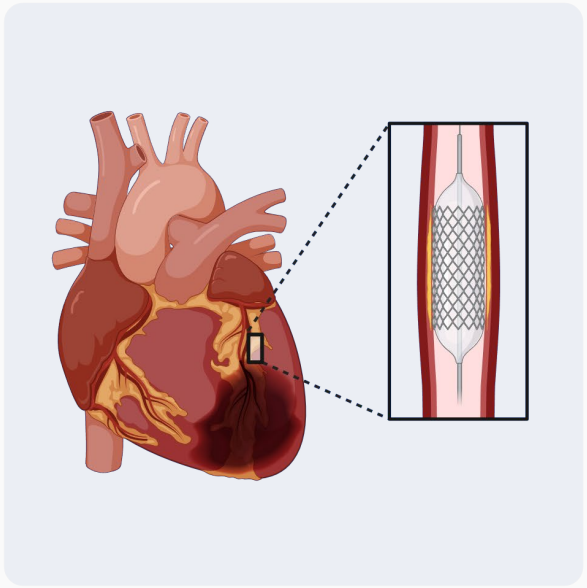



N Engl J Med **1981**;304:801

# Background & Rationale



More sensitive diagnostication of AMI



Revascularization - PCI

Modern secondary prevention

**Should beta-blockers be given routinely to post-MI patients without heart failure?**

# BETAMI-DANBLOCK: Study design

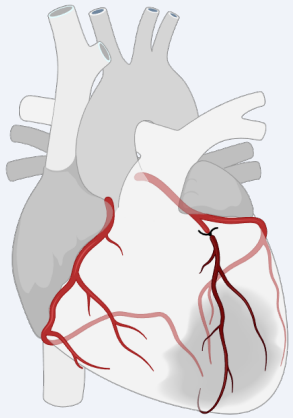
A randomized, open-label,
blinded end point evaluation superiority trial


Norway


Denmark

# BETAMI-DANBLOCK: Study population

## Inclusion criteria



- Myocardial infarction ≤14 days
- Mildly reduced or preserved LVEF (≥40%)
- Coronary revascularization *(BETAMI)*

## Exclusion criteria

- Indication/contraindication to beta-blocker therapy
- Heart failure
- Unsuitable for participation

# BETAMI-DANBLOCK: Endpoints

**Primary composite endpoint:**

All-cause mortality or MACE

- *Recurrent myocardial infarction*
- *Unplanned coronary revascularization*
- *Heart failure*
- *Ischemic stroke*
- *Malignant ventricular arrhythmias*

**Secondary endpoints:**

- Each component of the primary endpoint
- Hospitalizations for pacemaker implantation
- Second- or third-degree AV-block

# BETAMI-DANBLOCK: Statistical methods and sample size calculation

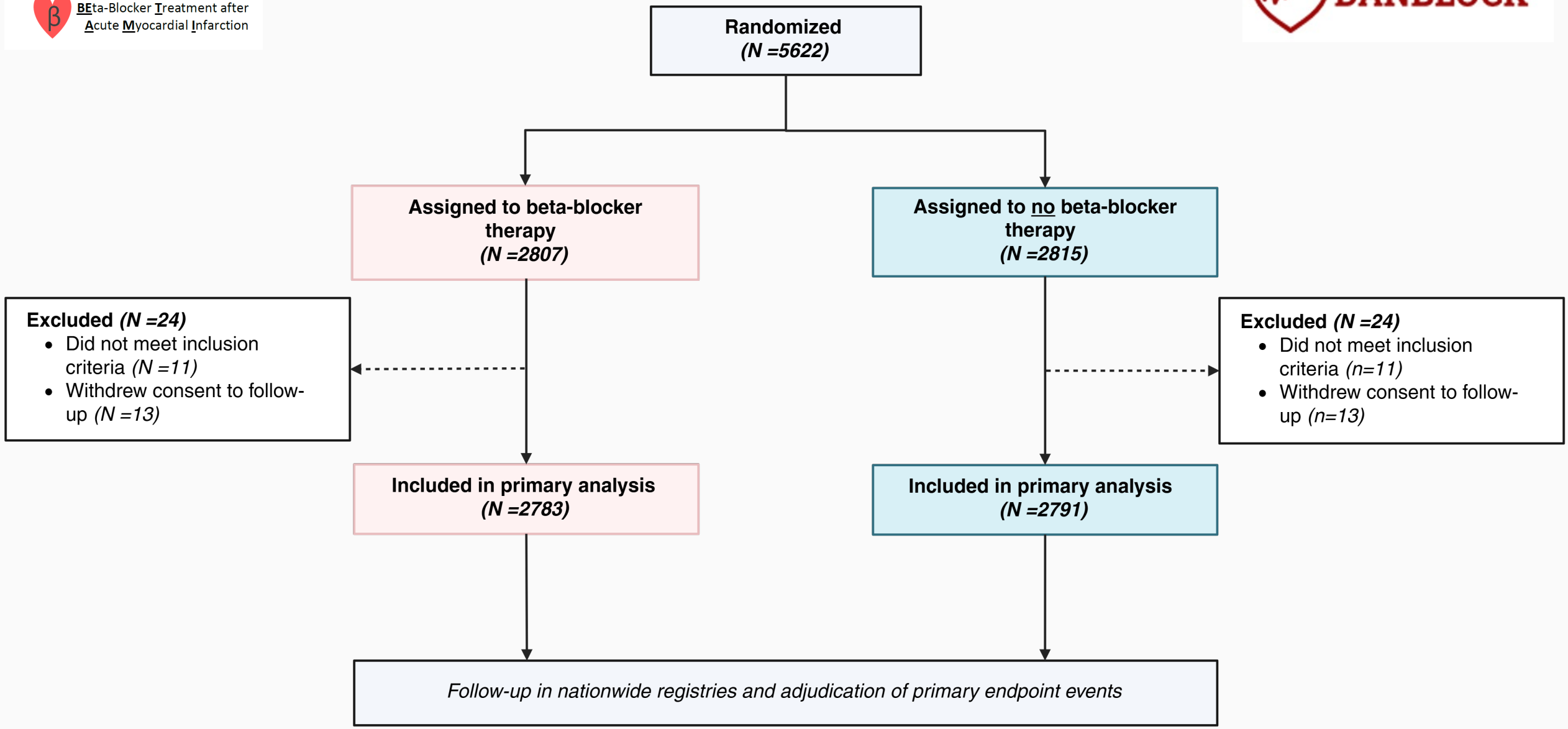
Prespecified analyses performed in the **intention-to-treat population**.

Power calculation based on the assumption that beta-blockers should prove **superiority** over no beta-blockers.

We estimated that approximately **950 primary end-point events** would provide the trial **80% power** to detect a treatment effect with a **hazard ratio of 0.83**.

# BETAMI-DANBLOCK: Results

# BETAMI-DANBLOCK: Study disposition



# BETAMI-DANBLOCK: Baseline Characteristics (I)

| Table 1. Characteristics of the Patients (N = 5574) | | |
|---|---|---|
| **Characteristic** | **Beta-Blockers (N=2783)** | **No Beta-Blockers (N=2791)** |
| Median age - yr (IQR) | 63 (55 - 71) | 62 (55 - 71) |
| Women - no./total no. (%) | 601 / 2783 (21.6) | 562 / 2791 (20.2) |
| Country - no./total no. (%) | | |
| Denmark | 1352 / 2783 (48.6) | 1355 / 2791 (48.5) |
| Norway | 1431 / 2783 (51.4) | 1436 / 2791 (51.5) |
| Risk factors - no./total no. (%) | | |
| Current smoker | 640 / 2279 (28.1) | 614 / 2259 (27.2) |
| Median Body Mass Index - $kg/m^2$ (IQR) | 28 (25 - 30) | 28 (25 - 31) |
| Hypertension | 1126 / 2783 (40.5) | 1150 / 2791 (41.2) |
| Diabetes mellitus | 332 / 2783 (11.9) | 363 / 2791 (13.0) |
| Hypercholesterolemia | 801 / 2775 (28.9) | 808 / 2787 (29.0) |
| Median low-density lipoprotein cholesterol - mmol/l (IQR) | 3.3 (2.6-4.0) | 3.3 (2.5-4.0) |
| Previous cardiovascular disease - no./total no. (%) | | |
| Coronary artery disease | 290 / 2783 (10.4) | 298 / 2791 (10.7) |
| Peripheral artery disease | 82 / 2777 (3.0) | 83 / 2790 (3.0) |
| Stroke | 81 / 2783 (2.9) | 74 / 2791 (2.7) |
| Atrial fibrillation/flutter | 52 / 2775 (1.9) | 57 / 2789 (2.0) |
| Prior beta-blocker therapy | 308 / 2775 (11.1) | 284 / 2788 (10.2) |

# BETAMI-DANBLOCK: Baseline Characteristics (II)

| Index MI - no./total no. (%) | Beta-Blockers (N=2783) | No Beta-Blockers (N=2791) |
|---|---|---|
| ST-elevation MI | 1329 / 2782 (47.8) | 1316 / 2791 (47.2) |
| LVEF 40-49% | 446 / 2778 (16.1) | 406 / 2791 (14.5) |
| In hospital course - no./total no. (%) | | |
| Percutaneous coronary intervention | 2582 / 2780 (92.9) | 2577 / 2785 (92.3) |
| Coronary-artery bypass grafting | 46 / 2780 (1.7) | 56 / 2785 (2.0) |
| No revascularization | 176 / 2783 (6.3) | 170 / 2791 (6.1) |
| Medication at discharge (≤30 days after MI) - no./total no. (%) | | |
| Aspirin | 2637 / 2783 (94.8) | 2656 / 2791 (95.2) |
| $P2Y_{12}$ receptor blocker | 2478 / 2783 (89.0) | 2463 / 2791 (88.2) |
| Anti-coagulants | 121 / 2776 (4.4) | 99 / 2787 (3.6) |
| ACE inhibitor or ARB | 1092 / 2776 (39.3) | 1217 / 2787 (43.7) |
| Statin | 2692 / 2776 (97.0) | 2719 / 2787 (97.6) |
| Ezetimibe | 363 / 2776 (13.1) | 339 / 2787 (12.2) |

# BETAMI-DANBLOCK: Follow-up

**Median follow-up:** 3.5 years (IQR 2.2-4.6)

**Adherence at 6 months:** 89% in the beta-blocker group and 89% in the no beta-blocker group

**Beta-blocker group:** Metoprolol used in 95%, median dose 50 mg (IQR 25-50)

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# BETAMI-DANBLOCK - PRIMARY RESULT

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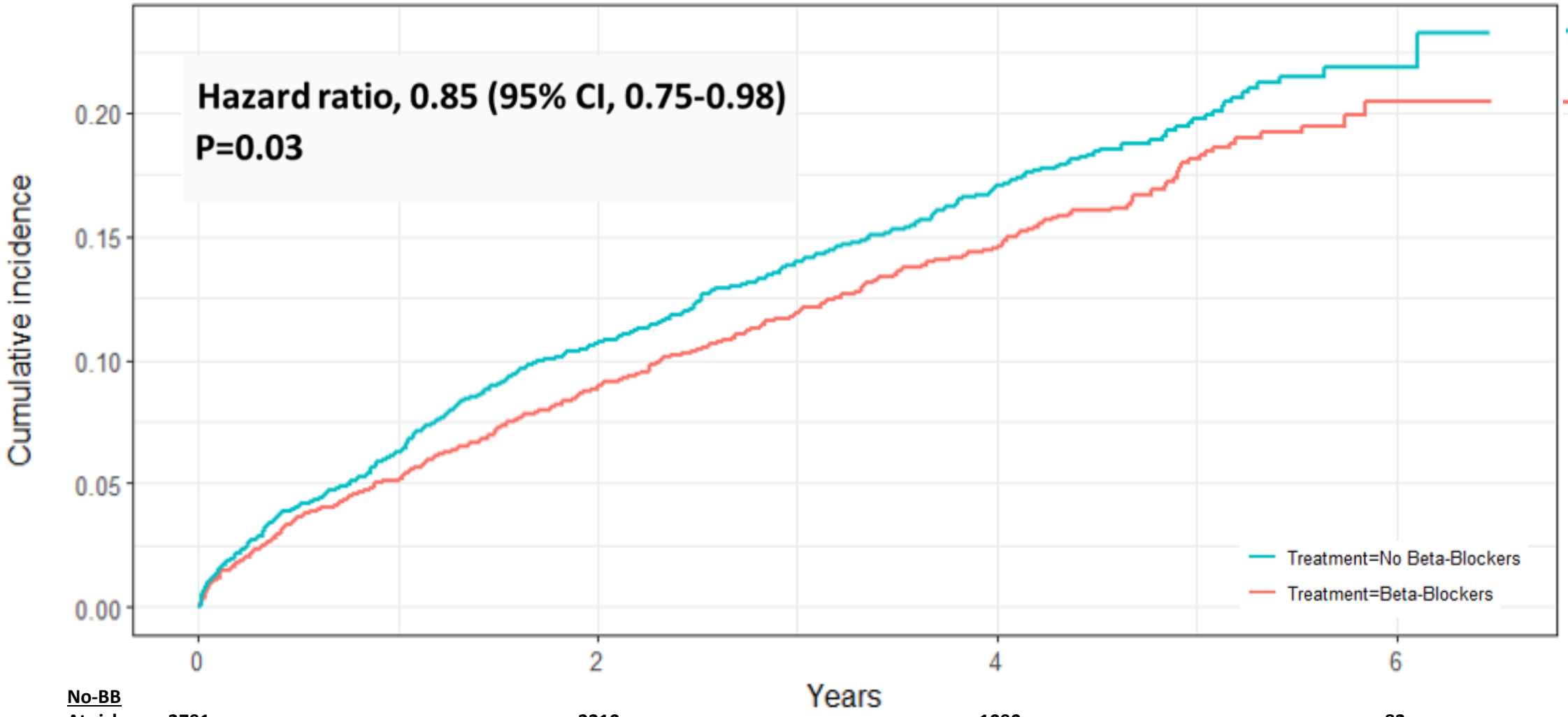
## All-cause Mortality or MACE




No BB

BB

Median follow-up 3.5 years

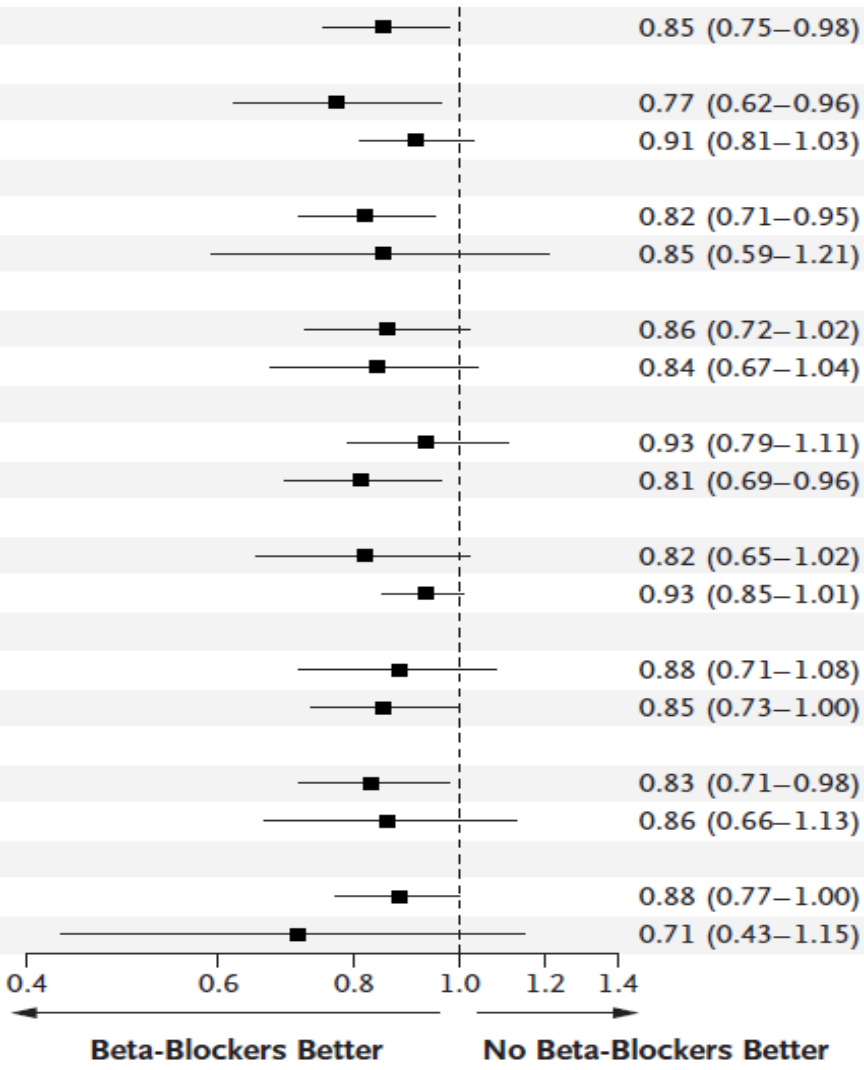
| | | | | |
|---|---|---|---|---|
| No-BB | | | | |
| At risk | 2791 | 2210 | 1090 | 82 |
| BB | | | | |
| At risk | 2783 | 2241 | 1114 | 95 |

# BETAMI-DANBLOCK - Primary and Secondary Endpoints

| End Point | Beta-Blockers (N=2783) | No Beta-Blockers (N=2791) | Hazard Ratio (95% CI) |
|---|---|---|---|
| | | *number (percent)* | |
| **Primary end point†** | | | |
| Composite of death from any cause, myocardial infarction, unplanned coronary revascularization, ischemic stroke, heart failure, or malignant ventricular arrhythmias‡ | 394 (14.2) | 454 (16.3) | 0.85 (0.75–0.98) |
| **Secondary end points** | | | |
| Death from any cause | 118 (4.2) | 124 (4.4) | 0.94 (0.73–1.21) |
| Myocardial infarction | 138 (5.0) | 186 (6.7) | 0.73 (0.59–0.92) |
| Unplanned coronary revascularization | 108 (3.9) | 110 (3.9) | 0.99 (0.76–1.29) |
| Ischemic stroke | 45 (1.6) | 35 (1.3) | 1.30 (0.84–2.03) |
| Heart failure | 42 (1.5) | 52 (1.9) | 0.78 (0.52–1.18) |
| Malignant ventricular arrhythmias‡ | 15 (0.5) | 18 (0.6) | 0.82 (0.42–1.64) |
| Implantation of a pacemaker or second- or third-degree atrioventricular block | 49 (1.8) | 49 (1.8) | 1.00 (0.67–1.49) |
| **Safety end point** | | | |
| Composite of death from any cause, myocardial infarction, heart failure, or malignant ventricular arrhythmia at 30 days | 21 (0.8) | 32 (1.1) | |

# BETAMI-DANBLOCK - Subgroup Analysis

| Subgroup | Beta-Blockers | No Beta-Blockers | Hazard Ratio (95% CI) |
|---|---|---|---|
| | *no. of events/total no. of patients (%)* | | |
| All patients | 394/2783 (14.2) | 454/2791 (16.3) | 0.85 (0.75–0.98) |
| Sex | | | |
| Female | 89/601 (14.8) | 107/561 (19.1) | 0.77 (0.62–0.96) |
| Male | 305/2182 (14.0) | 347/2230 (15.6) | 0.91 (0.81–1.03) |
| Age | | | |
| <70 yr | 225/2001 (11.2) | 281/2029 (13.8) | 0.82 (0.71–0.95) |
| ≥70 yr | 169/782 (21.6) | 173/762 (22.7) | 0.85 (0.59–1.21) |
| Country | | | |
| Norway | 204/1431 (14.3) | 235/1436 (16.4) | 0.86 (0.72–1.02) |
| Denmark | 190/1352 (14.1) | 219/1355 (16.2) | 0.84 (0.67–1.04) |
| Type of myocardial infarction | | | |
| NSTEMI | 230/1453 (15.8) | 246/1475 (16.7) | 0.93 (0.79–1.11) |
| STEMI | 164/1330 (12.3) | 208/1316 (15.8) | 0.81 (0.69–0.96) |
| Left ventricular ejection fraction | | | |
| 40–49% | 82/446 (18.4) | 95/406 (23.4) | 0.82 (0.65–1.02) |
| ≥50% | 312/2333 (13.4) | 359/2385 (15.1) | 0.93 (0.85–1.01) |
| Beta-blocker dose | | | |
| <50 mg | 112/801 (14.0) | 454/2791 (16.3) | 0.88 (0.71–1.08) |
| ≥50 mg | 257/1813 (14.2) | 454/2791 (16.3) | 0.85 (0.73–1.00) |
| Hypertension | | | |
| No | 198/1656 (12.0) | 232/1642 (14.1) | 0.83 (0.71–0.98) |
| Yes | 196/1127 (17.4) | 222/1149 (19.3) | 0.86 (0.66–1.13) |
| Diabetes | | | |
| No | 326/2451 (13.3) | 364/2428 (15.0) | 0.88 (0.77–1.00) |
| Yes | 68/332 (20.5) | 90/363 (24.8) | 0.71 (0.43–1.15) |



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# CONCLUSIONS

This randomized trial of beta-blocker therapy versus no beta-blocker therapy was carried out in 5574 patients with an MI and preserved or mildly reduced LVEF.

Long-term beta-blocker therapy, initiated within 14 days of MI, reduced the primary endpoint of death from any cause or major adverse cardiovascular events.

In this adequately powered study, beta-blockers proved superior to no beta-blockers, supporting their continued role in secondary prevention after myocardial infarction.

## Executive Steering Committee

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BETAMI-sites:

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DANBLOCK-sites:

Olsen MH (Holbæk), Maeng M (Aarhus), Jensen SE (Aalborg), Lambrechtsen J (Svendborg), Bovin A (Vejle), Christiansen MK (Horsens), Krarup NT (Viborg), Mikkelsen D (Slagelse), Schou JB (Amager), Gislason G (Gentofte), Abdulla JAM (Glostrup), Mouridsen MR (Herlev), Bertelsen MLN, Hove, JD (Hvidovre), Schierbeck L (Hillerød) Snoer M (Roskilde), Egholm G (Odense), Thomsen KK (Esbjerg), Jadou G (Aabenraa), Poenaru MP (Kolding), Bøttcher M (Herning), Stæhr PB (Hjørring), Frost L (Silkeborg), Larsen J (Næstved), Prescott EIB (Bispebjerg), Kristensen KS (Rønne).

# BETAMI-DANBLOCK

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Beta-Blockers after Myocardial Infarction in Patients without Heart Failure

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